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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,249	10/17/2001	Michele Fiscella	PT054P1	4118

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EXAMINER	
SPIEGLER, ALEXANDER H	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,249	FISCELLA ET AL.	
	Examiner	Art Unit	
	Alexander H. Spiegler	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12,13,17,18 and 23-42* is/are pending in the application.

4a) Of the above claim(s) *12,13,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

1. This action is in response to Applicant's response, filed on October 22, 2003. Currently, Claims 12-13, 17-18 and 23-42 are pending, Claims 12-13 and 17-18 have been withdrawn as being drawn to a non-elected invention (see MPEP § 821), and Claims 23-42 are rejected herein.

Election/Restrictions

2. Applicant's election with traverse of Group I (directed to nucleic acids, which is now reflected by newly added Claims 23-42) and polynucleotides encoding SEQ ID NO: 10 are acknowledged.

Applicants traversal is on the ground(s) that Groups I-IX are directed to subject matter that is closely interrelated and therefore examination of all of the groups would not place an undue burden on the Examiner. This is not found persuasive because it is maintained that undue burden would be required to examine the claims of Groups I-IX. Restriction of related inventions is proper if it can be shown that the inventions have a different classification, or have acquired a separate status in the art or have a different field of search (see MPEP 808.02). The claims of groups I-IX have acquired a separate status in the art as recognized by their different classification and as recognized by their divergent subject matter. A search of the distinct inventions would not be co-extensive as evidenced by the requirement for searching different keywords, by the different classification of each invention, and because a sequence search for nucleic acids and polypeptides (for example) requires a different structural search, as a nucleic acid search requires the search of nucleotides, whereas a polypeptide search requires the search of amino acids. Furthermore, it is maintained that each of the inventions are distinct for the

reasons discussed in the previous Office action. Accordingly, because undue burden would be required to examine each of the claimed inventions, the requirement is still deemed proper, and is therefore maintained.

CRF/Sequence Notes

3. The Sequence Listing filed in this application complies with the requirements of 37 CFR 1.821-1.825 and has been entered.

Specification

4. The disclosure is objected to because the title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 23-42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

The specification teaches SEQ ID NO: 5 (which encodes SEQ ID NO: 10) is "GENE NO: 4" (see page 30). Specifically, the specification teaches "translation products of this gene share sequence homology with numerous basement membrane heparan sulfate proteoglycans, including perlecan from Mus musculus (See Genbank Accession AAA39911)". (See page 30, paragraph 83). However, the specification does not teach what the sequence homology is between the translation products of this gene and the "numerous" basement membrane heparan sulfate proteoglycans. After describing some of the properties of a specific heparan sulfate

proteoglycan, perlecan (of which no sequence homology is shown with the instant invention), the specification concludes, "based upon the homology between these proteins, *it is expected that the translation products of this gene will share at least some biological activities with these proteins*." (emphasis added) (see page 31, paragraph 83). That is, despite the lack of evidence of specific homology between the protein encoded by Gene 4 and heparan sulfate proteoglycans, the specification concludes that these proteins will share "at least some biological activities". The specification does not discuss what the "at least some biological activities" might consist of. Accordingly, with respect to the specification's assertion of homology with the protein encoded by Gene 4 and that of heparan sulfate proteoglycans, the specification has not identified any specific biological activity for the protein encoded by Gene 4.

The specification also states, "translation products corresponding to this gene also share sequence homology with an agrin-related protein from Gallus gallus (See Genbank Accession AAA48586). (See page 31, paragraph 84). However, the specification does not teach what the sequence homology is between the translation products of this gene and "an agrin-related protein from Gallus gallus". After describing some of the properties of the protein from Gallus gallus (of which no sequence homology is shown with the instant invention), the specification concludes, "based upon the homology between these proteins, *it is expected that the translation products of this gene will share at least some biological activities with these proteins*." (emphasis added) (see page 31, paragraph 84). That is, despite the lack of evidence of specific homology between the protein encoded by Gene 4 and "an agrin-related protein from Gallus gallus", the specification concludes that these proteins will share "at least some biological activities". The specification does not discuss what the "at least some biological activities"

might consist of. Accordingly, with respect to the specification's assertion of homology with the protein encoded by Gene 4 and that of "an agrin-related protein from Gallus gallus", the specification has not identified any specific biological activity for the protein encoded by Gene 4.

The specification then states, "the gene encoding the disclosed CDNA is thought to reside on chromosome 5. Accordingly, polynucleotides related to this invention have uses, such as, for example, as a marker in linkage analysis for chromosome 5." (See page 31, paragraph 85).

MPEP 2107.01 states:

> A "specific utility" is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention... a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target.

Accordingly, the asserted utility of a chromosome marker and that the protein encoded by Gene 34 shares "at least some" *unspecified* "biological activities" with other proteins (a property applicable to a broad class of polynucleotides encoding polypeptides) is not considered to be a specific utility.

Next, the specification states, "this gene is expressed in myosarcoma and testes tissues, and to a lesser extent in lung carcinoma, human adrenal gland tumor, and fetal liver/spleen tissues." (See page 31, paragraph 87). However, the specification does not teach or demonstrate any evidence of differential expression (e.g., between normal or cancer cells or tissues) or any other data that specifically correlates the expression of this gene and any disease or condition. Specifically, even if this gene is expressed in myosarcoma and testes tissues, the specification does not teach whether this gene is expressed, for example, in normal muscle cells or in

cancerous testes tissue. Therefore, the limited expression data provided by the specification does not specifically assert, for example, that the claimed gene is only expressed in a cancer cell or tissue and not in a normal cell or tissues. That is, while the specification asserts some expression data, it is not clear whether other cells/tissues were tested, what cells/tissues were tested, whether they were diseased or normal samples, etc., and therefore, the specification does not teach a reasonable or specific correlation between the expression of the claimed gene and any condition or disease. Furthermore, the assertion that the gene is expressed "to a lesser extent" is also vague, since it is not clear as to what "a lesser extent" actually means, let alone whether expression "to a lesser extent" is significant for screening/assayable purposes.

Given the limited expression data, the specification states,

> "polynucleotides and polypeptides of the invention...are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include but are not limited to: diseases and/or disorders of the musculo-skeletal and male reproductive systems."

(See page 32, paragraph 88).

The asserted utility of using polynucleotides or polypeptides for diagnosis of "diseases and/or disorders of the musculo-skeletal and male reproductive system" is not considered to be specific, since "diseases and/or disorders" of the "musculo-skeletal and male reproductive system" comprise a general classes of possible diseases and/or disorders which could comprise hundreds of possible diseases and/or disorders. Accordingly, because the specification indicates that the claimed polynucleotide may be useful in diagnosing *unspecified* disorders, and therefore, not in diagnosing any specific musculo-skeletal and male reproductive system disease or disorder, the claimed utility is not specific. See MPEP 2107.01 and the Utility Guidelines. Alternatively, this claimed utility would also not be considered to be substantial, since the skilled

artisan would have to carry out further research to identify or reasonably confirm a "real world" context of use, e.g., diagnosis a specific musculo-skeletal and male reproductive system disease or disorder, in light of the specification's lack of evidence regarding any reasonable or specific correlation between the expression of the claimed gene and any disease and/or disorder. See MPEP 2107.01 and the Utility Guidelines.

The specification also states, "Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s)." (See page 32, paragraph 88) This asserted utility is not considered to be specific because no specific DNA target is disclosed (see above and MPEP 2107.01).

The specification states further,

> For a number of disorders of the above tissues or cells, particularly of the musculo-skeletal and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., musculo-skeletal, reproductive, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

(page 32, paragraph 88). However, the specification does not teach whether the increased or decreased expression of this gene is detected in a specific disorder relative to the standard expression level in healthy tissue or bodily fluid from an individual not having the disorder. Thus, this passage does not define a substantial utility, as the skilled artisan would have to experiment to find a correlation between the claimed gene and a disease or disorder. See MPEP 2107.01. Furthermore, the general statement of using gene expression data for the comparison of diseased samples versus normal samples (e.g., musculo-skeletal, reproductive, cancerous and

wounded tissues) is applicable to any gene, and therefore, this utility is not considered to be specific.

On page 32, paragraph 88, the specification states,

> The tissue distribution in myosarcoma and testes tissues, and the homology to perlecan and an agrin-related protein, indicates that polynucleotides, translation products, and antibodies corresponding to this gene are useful for the diagnosis, detection and/or treatment of diseases and/or disorders of the musculo-skeletal and reproductive systems.

This assertion also lacks specific and substantial utility for several reasons. First, no homology data is present in the specification, the specification only teaches that the translation products of this gene share "some" biological activity (of which no activity is taught), and no specific disease and/or disorder of the musculo-skeletal and reproductive systems are discussed. Second, the specification does not provide any comparative expression data of normal or diseased samples of the claimed gene. Finally, the skilled artisan would have to carry out further experimentation to correlate expression of the claimed gene and disease.

The specification also asserts,

> Translation products corresponding to this gene are useful in treating diseases and/or disorders of the musculo-skeletal system, particularly such disorders as atrophy of muscle tissue due to nerve trauma. degenerative, metabolic, or inflammatory neuropathy, peripheral neuropathy, or damage to nerves caused by environmental toxins or drugs. This is particularly useful where the muscle atrophy is due to motor neuronopathy, metabolic stress or nutritional insufficiency, chronic disorders of the immune system, muscular dystrophy syndrome, congenital myopathy or acquired myopathy.

(page 32, paragraph 90). This assertion of treating diseases and/or disorders lacks specific utility because no specific disease or disorder is discussed. The specification states general classes of disease/disorder (e.g., disorders as atrophy of muscle tissue due to nerve trauma. degenerative, metabolic, or inflammatory neuropathy, peripheral neuropathy, or damage to nerves caused by environmental toxins or drugs), but does not teach any specific disorder within one of these

general classes of diseases/disorders. Furthermore, this asserted utility is also not substantial because this passage does not identify a specified disease within one of the broad, general classes of diseases above. See MPEP 2107.01 I (B). Furthermore, the skilled artisan would have to carry out further experimentation to correlate the claimed gene and a particular disease or disorder, and determine whether the translation products of this gene can be used in treatment of a particular disease or disorder.

On page 32, paragraph 91, the specification states,

> More generally, the tissue distribution in testes tissue indicates that translation products corresponding to this gene are useful for the treatment and/or diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, translation products corresponding to this gene are useful in the treatment of male infertility and/or impotence.

While the asserted utility of treating and/or diagnosis of conditions concerning proper testicular function (e.g., sperm maturation, male infertility and/or impotence) may be specific, they are not substantial. The specification does not teach any correlation with the treatment and/or diagnosis of the claimed gene or its translation product and these conditions. The specification only suggests that this gene is expressed in testes tissue, but does not teach any other expression data. Furthermore, the specification does not teach any linkage between expression data and the conditions specified, such as male infertility, sperm maturation or impotence. Accordingly, because the skilled artisan would have to carry out further experimentation to determine whether gene expression is correlated to male infertility, sperm maturation or impotence, and furthermore, whether gene expression of the claimed gene is correlated with any of these conditions, these utilities are not substantial.

Page 32, paragraph 91, also asserts, "translation products corresponding to this gene are also useful in assays designed to identify binding agents, as such agents (antagonists) are useful as male contraceptive agents." This asserted utility lacks specific and substantial utility because no specific "male contraceptive agent" is specified, nor discussed, and furthermore, the skilled artisan would have to carry out further experimentation to determine what the translation products can bind to and act as male contraceptive agents. That is, absent any guidance in the specification as to any specific assay, the skilled artisan would have to experiment to determine what the translation products can be used to assay for.

Page 32, paragraph 91, also states, "translation products of this gene are believed to be useful in the treatment and/or diagnosis of testicular cancer". While this asserted utility is specific, it is not substantial, as the specification does not teach any correlation between translation products of the claimed invention and testicular cancer. Specifically, the specification only teaches the claimed gene is expressed in testes tissue; however, it does not specify the gene was expressed in cancerous tissue. That is, the skilled artisan would have to carry out further experimentation to determine whether there is any correlation between the translation products of gene 4 and testicular cancer.

Finally, page 32, paragraph 91, asserts,

> [T]hese translation products may be expressed in other specific tissues or organs where they may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

These asserted utilities are neither specific nor substantial because the specification does not teach how the translation products play functional roles or what specific functional role they play

in the processes discussed. Therefore, the skilled artisan would have to carry out further experimentation to determine what role the translation products may play in these processes.

The specification also states,

> Furthermore, the tissue distribution in cancerous and fetal tissues indicates that translation products corresponding to this gene are useful for the diagnosis and treatment of cancer and other proliferative disorders. Expression within embryonic tissue and other cellular sources marked by proliferating cells suggests that translation products of this gene may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders....translation products of this gene may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy.

(page 33, paragraph 92). These utilities are also neither specific nor substantial. First, the specification only teaches that gene 4 is expressed "to a lesser extent" in fetal liver/spleen tissues. As stated above, the assertion that gene 4 is expressed "to a lesser extent" is vague, since it is not clear as to what "a lesser extent" actually means, let alone whether expression "to a lesser extent" is significant for screening/assayable purposes. Therefore, the skilled artisan would have to carry out further experimentation to determine gene 4's level of expression, and how that relates to any particular cancer or proliferative disorder. Furthermore, with respect to the assertion that the translation products of gene 4 "may" play a role in several processes is not considered to be specific or substantial because the specification does not teach what role or how the translation products play a role in these processes, and therefore, the skilled artisan would have to experiment to determine the role played by gene 4's translation products.

The specification also asserts,

> Alternatively, translation products corresponding to this gene may be involved in hyperproliferation, by way of a non-limiting hypothesis, through abnormal upregulation of growth factors, or may be involved in enhancing metastasis, by way of a non-limiting hypothesis, through adhesion to neighboring tissues or extracellular matrices, or by enhancing angiogenesis.

(page 33, paragraph 93). Here, the specification hypothesizes on what the translation products "may be involved" with, however, the specification does not provide any data to support such hypotheses. Specifically, the specification does not provide any data relating the translation products of gene 4 and growth factors, enhancing metastasis or enhancing angiogenesis. More specifically, the specification does not teach how these hypotheses translate into a specific or substantial utility.

Finally, the specification states, "translation products corresponding to this gene...may show utility as tumor markers and/or immunotherapy targets for the above listed tissues." (page 33, paragraph 94). Again, as stated above, this assertion lacks, at least, a substantial utility, as the specification does not specifically or reasonably correlate gene 4, and any disease or condition. Therefore, the skilled artisan would have to carry out further experimentation to determine what tumor or immunotherapy target the translation products of gene 4 can be used for.

Based on the foregoing analysis, the claimed invention is not supported by either a specific or substantial utility, or alternatively, a well-established utility, as the specification does not teach a specific or reasonable correlation between the gene (or its translation product) and any specific biological activity or use in disease/disorder detection or treatment.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 23-42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

9. No Claims are allowable.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alexander H. Spiegler whose telephone number is (571) 272-0788. The examiner can normally be reached on Monday through Friday, 7:00 AM to 3:30 PM.

If attempts to reach the examiner are unsuccessful, the primary examiner in charge of the prosecution of this case, Carla Myers, can be reached at (571) 272-0747. If attempts to reach Carla Myers are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at (571) 272-0782. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alexander H. Spiegler
January 21, 2004

CARLA J. MYERS
PRIMARY EXAMINER